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Successful Recollection of Remote Autobiographical Memories by Amnesic Patients with Medial Temporal Lobe Lesions

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Summary

Current views about the organization of human memory make strikingly different predictions about the integrity of remote autobiographical memory following damage to the medial temporal lobe. We have carried out a detailed analysis of narrative content in memory-impaired patients for whom neuropsychological and neuroanatomical information is available. All eight patients were able to recall detailed memories from their early lives. The recollections of the patients and the recollections of 25 matched controls contained the same number of details (±5%) and were also similar by several other measures. The results support the view that autobiographical memories eventually become independent of the medial temporal lobe as time passes after learning. A number of other considerations suggest that the neocortex ultimately supports the capacity for recollecting remote autobiographical memory.

Introduction

The phenomenon of temporally limited retrograde amnesia has been described in the clinic and in the laboratory for more than 100 years (Ribot, 1881; Hodges, 1994; Kopelman and Kapur, 2001; Squire et al., 2001). In studies of both humans and experimental animals with damage to the hippocampus or related medial temporal lobe structures, memory loss is often graded within very long-term memory, such that remote memory is spared relative to recent memory. This pattern of findings has usually been interpreted as support for a process of memory consolidation or reorganization that occurs gradually within long-term memory, with the result that medial temporal lobe structures become less important as time passes after learning (Squire et al., 1984; McGaugh, 2000).

There is disagreement about the conditions under which temporally limited retrograde amnesia occurs and about the nature of memory consolidation (Spiers et al., 2001). An important focus of discussion concerns the capacity for recollecting autobiographical episodes from one's personal past. Memories of autobiographical events are often complex and richly detailed narratives, and they have the defining feature of being unique to a particular time and place. In this sense, autobiographical recollections are the quintessential example of episodic memory and are distinct from the factual knowledge that comprises semantic memory (Tulving, 1983).

One view has been that autobiographical memory, like semantic memory, gradually becomes independent of the medial temporal lobe through a process of consolidation (Squire and Alvarez, 1995). A quite different view is that episodic memory is not subject to memory consolidation and remains dependent on the medial temporal lobe as time passes (Fujii et al., 2000). By this view, the maintenance and reconstruction of episodic memory depend on the integrity of the hippocampus and related medial temporal lobe structures as long as the memories persist. These two views make opposite predictions about the status of early autobiographical memories in patients with medial temporal lobe damage. By the first view, remote autobiographical memory should be intact. By the second view, remote autobiographical memory should be impaired.

Earlier studies suggested that remote autobiographical memory can be intact after damage to the hippocampal region or adjacent cortex (Zola-Morgan et al., 1986; Rempel-Clower et al., 1996; Reed and Squire, 1998) and that more recent autobiographical memory is impaired (Beatty et al., 1987; Schnider et al., 1995; Mayes et al., 1997; Reed and Squire, 1998; Henke et al., 1999; Kapur and Brooks, 1999). Yet, patients have also been described who appear to have difficulty recalling autobiographical episodes from all periods of their life, including the most remote time periods tested (Hirano and Noguchi, 1998; Moscovitch et al., 2000; Cipolotti et al., 2001).

There appear to be two ways to reconcile the available data. One possibility is that impairment of remote autobiographical memory was not detected in the earlier studies because the assessment of the quality of remote recollections was insufficiently sensitive (e.g., scoring was based on a 0 to 3 scale). A patient's recollection might receive a full score of 3 but nevertheless contain less detail and less context than the recollection of a healthy individual. Accordingly, more sensitive tests might reveal impairment, such as tests in which the total narrative content is evaluated (e.g., the number of details contained in a narrative [Levine et al., 2002]). A second possibility is that the status of remote autobiographical memory will be clarified when adequate anatomical data are available for the patients under study. For example, patients with restricted hippocampal damage or damage limited to the medial temporal lobe may have an intact capacity for recollecting remote autobiographical episodes, and patients reported to be deficient at autobiographical recollection might have significant damage in addition to damage in the medial temporal lobe.

We have carried out a detailed analysis of the narrative content of autobiographical recollections in memory-impaired patients for whom considerable neuropsychological and neuroanatomical information is available (Figure 1). Six of the patients have moderately severe memory impairment and damage limited primarily to the hippocampal formation, and two patients have profound memory impairment and more extensive medial temporal lobe damage (Figure 2). All eight patients were able

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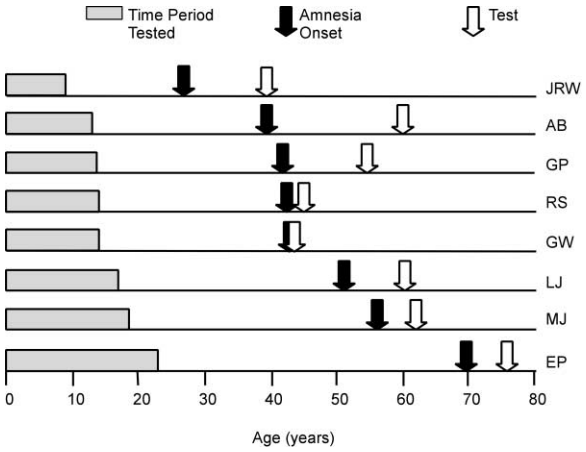

Figure 1. A Timeline for Each of the Eight Patients Showing the Time Period from which the Patient Was Asked to Draw Remote Autobiographical Memories, the Patient's Age at the Onset of Amnesia, and Age at the Time of Testing

The horizontal bar to the left indicates the time period tested, the black arrow indicates age at the onset of amnesia, and the white arrow indicates age at testing. Controls matched to each patient were asked to draw memories from an equivalent portion of their lives.

to recollect detailed memories from their early lives. The recollections of the patients and the recollections of matched controls (n = 25) contained the same number of details (±5%) and were similar on several other measures as well.

Results

Scoring Narratives on a 0 to 3 Scale

The autobiographical narratives were first evaluated on a 0 to 3 scale. Because the distribution of scores was positively skewed, nonparametric statistics were used to evaluate differences between groups. For study 1 and study 2, the patients and controls were able to provide unique autobiographical memories (scoring 3 points) in response to most of the 24 cue words (Figure 3A, five patients obtained a 3 point score in response to 88.3% of the cue words; 19 controls, 94.9%; $U = 34$, $p > 0.10$; Figure 3B, three patients, 90.6%; six controls, 96.5%; $U = 5.5$, $p > 0.10$; average overall score: eight patients = 2.8; 25 controls = 2.9, $p > 0.10$).

Scoring Narratives for Detail

All the narratives that were awarded 3 points were next scored for the amount of detail they contained. Figure 4 shows the number of episodic and semantic details per narrative reported by the participants in the two studies. For both patients and controls, approximately two-thirds of the total details that were recollected were scored as episodic details, and one-third were scored as semantic details. With respect to episodic details (Figures 4A and 4B), the patients produced an average of 18.8 details per narrative, and the controls produced 17.9 details. There was no difference between groups ($p > 0.10$), no difference between the two studies ($p > 0.10$), and no group × study interaction ($p > 0.10$).

With respect to semantic details (Figures 4C and 4D), the patients produced on average 9.7 details per narrative, and the controls produced 10.0 details ($p > 0.10$). The participants in study 1 reported a greater number of semantic details than the participants in study 2 ($F_{(1,29)} = 6.6$, $p < 0.05$). However, there was no group effect ($p > 0.10$) and no group × study interaction ($p > 0.10$). These results indicate that amnesic patients, even patients with large medial temporal lobe lesions (E.P. and G.P.), were able to recall detailed autobiographical memories from their early life.

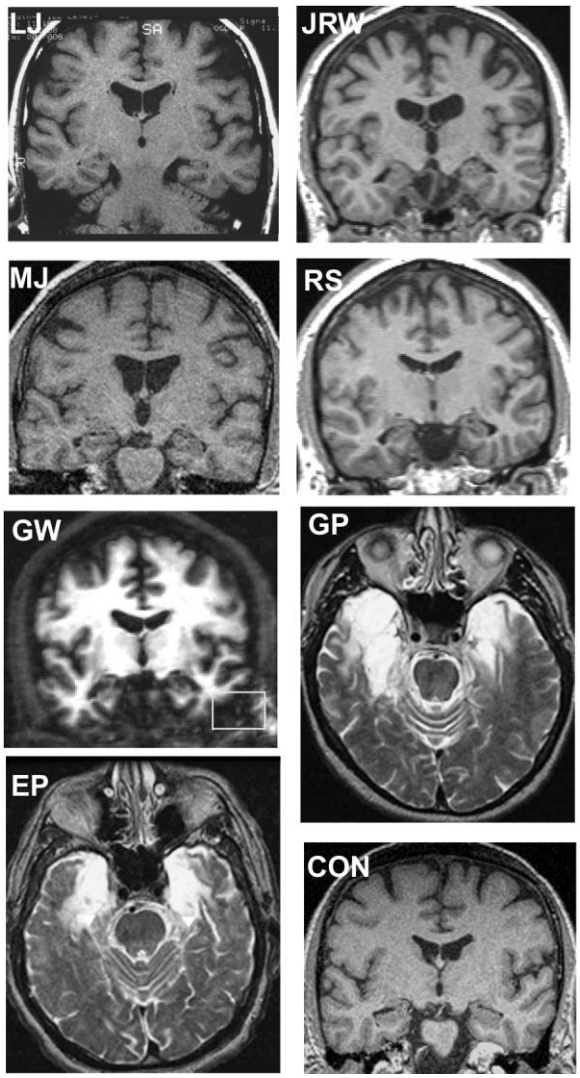

Figure 2. Magnetic Resonance Images Showing the Extent of Temporal Lobe Damage for Seven of the Eight Amnesic Patients and a Healthy Control

For five patients who have damage limited primarily to the hippocampal region (L.J., M.J., G.W., J.R.W., and R.S.) and one control (CON, aged 56 years), the images are T1-weighted coronal sections taken at the level of the anterior hippocampus. An imaging artifact is visible in the region of G.W.'s left lateral temporal lobe (Box). For two patients with more extensive medial temporal lobe damage (E.P. and G.P.), the images are T2-weighted axial sections through the temporal lobe. See text for detailed descriptions of the lesions.

Repetition of Details

The narratives provided by the patients and controls were not identical in every respect. The patients but not

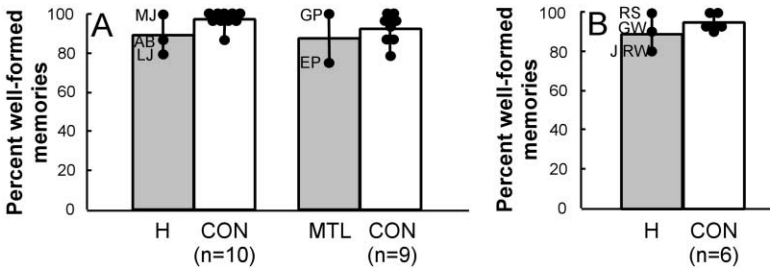

Figure 3. Performance on a Test of Remote Autobiographical Memory

Participants were given 24 cue words (e.g., river, bottle, nail) and asked to recollect a specific event that involved the word. Patients were asked to recall events from the first third of their life before the onset of amnesia, and controls were asked for events from the same portion of their life. Tape-recorded narratives were scored (0 to 3) for how well they described an event that was specific to time and place. Panels (A) (first study) and (B) (second study) show the percentage of narratives given a 3 point score after prompting. The two studies were identical, except that different interviewers were used. Each participant is represented by a filled circle, and patients are identified by their initials. H, patients with lesions limited primarily to the hippocampal region; MTL, postencephalitic patients with large medial temporal lobe lesions; CON, controls.

the controls tended to repeat details within a narrative (Figure 5), presumably because their amnesia made it difficult, as their narratives progressed, to remember what had already been said. Patients averaged 3.3 repetitions per narrative, and controls averaged 1.4 repetitions per narrative ($F_{(1,29)} = 7.9$, $p < 0.01$). This difference between groups was due largely to the performance of patients E.P. and G.P. (without these two patients, the group difference was not significant, 2.3 versus 1.4, $F_{(1,27)} = 3.0$, $p = 0.10$). These two patients are also the most severely amnesic of the patient group and have the most extensive medial temporal lobe damage, consistent with the idea that the repetitions were due to anterograde amnesia.

Latency and Duration of Narratives

The patients and controls required a similar amount of time to begin their narrative recollections, and once begun, the two groups took a similar amount of time to report their recollections (Figure 6). Overall, participants in study 1 took longer to begin their narratives than participants in study 2 ($F_{(1,29)} = 8.1$, $p < 0.01$), perhaps because the participants in study 1 were older than the participants in study 2 or perhaps because of differences in the styles of the interviewers who conducted the two studies. In any case, the patients and controls performed similarly, and there was no group $\times$ study interaction ($p > 0.10$). Similarly, the average duration of the narratives was longer in study 1 than in study 2 ($F_{(1,29)} = 16.2$, $p < 0.001$). Nevertheless, the two groups performed similarly ($p > 0.10$), and there was no group $\times$ study interaction ($p > 0.10$).

Prompts

Figures 7A and 7B show the number of prompts given by the interviewer before a narrative recollection was begun. The two groups received a similar number of prompts to begin their narratives ($p > 0.10$). Further, there was no difference between the two studies ($F_{(1,29)} = 1.6$, $p > 0.10$) and no group $\times$ study interaction ($p > 0.10$).

Figures 7C and 7D show the number of prompts given by the interviewer during the narrative recollections. More prompts were given to the patient group than to the controls ($F_{(1,29)} = 5.0$, $p < 0.05$). Patients were given an average of 6.4 prompts per narrative, and controls were given 4.8 prompts per narrative. This difference between groups was mainly due to the extra prompts

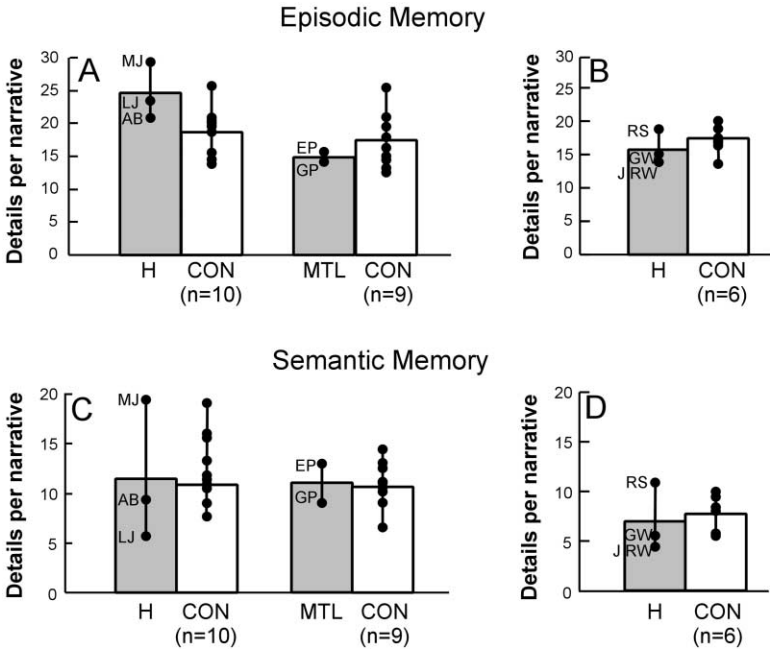

Figure 4. The Number of Details Contained in Remote Autobiographical Memories

Panels (A) (first study) and (B) (second study) show the mean number of details per narrative that described specific events (episodic memory). Panels (C) (first study) and (D) (second study) show the mean number of details per narrative that were recounted as part of an autobiographical memory but were not unique to a specific event (semantic memory). Abbreviations as in Figure 3.

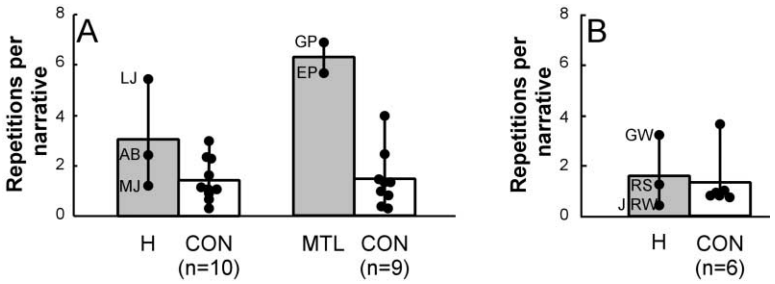

Figure 5. The Number of Times that Patients and Controls Repeated the Same Detail in Their Recollections

Repetitions were not counted in the tally of total details shown in Figure 4. Abbreviations as in Figure 3.

given to patients E.P. and G.P. (without these two patients, the group difference, 5.7 versus 4.8 prompts per narrative, was not significant, $F_{(1,27)} = 1.7$, $p > 0.10$). These two patients are also the most severely amnesic of the patient group, and they seemed to require additional support during their interviews to remain on task.

The Validity of Narrative Recollections as Memories

For all eight amnesic patients and six of the controls, an effort was made to determine the validity of the recollections. At a substantial interval after the initial interview (median = 14 months; range = 1–61 months), these 14 participants were interviewed again. The rationale was that participants (and especially the patients) should have difficulty answering questions about a narrative that they had produced previously, if the narrative was largely manufactured at the time of the first interview rather than recollected from memory. Accordingly, for each well-formed narrative recollection that had been reported previously (maximum = 24), participants were provided with two cues about the content of the original narrative and were then asked four specific questions about the narrative. For example, patient E.P. was asked about the incident transcribed in Figure 8 by telling him that he had described an incident involving a *grass fire* that occurred on his *father's property in Castro Valley*. He was then asked: "What did your father do when he saw the fire?" as well as three other questions. When at least three of the questions elicited the same information that was contained in the original narrative, the narrative was considered confirmed. The two groups performed similarly. Across all the recollections, the patients answered an average of 3.4 questions out of 4 in a manner consistent with their earlier narratives, and the controls answered 3.5 questions in a consistent manner. Overall, 88.0% of the patient recollections and 93.4% of the control recollections were considered to be confirmed ($t_{(12)} = 1.26$, $p > 0.10$).

It is worth noting that 5 of the 8 amnesic patients and 17 of the 25 controls were unable to report a well-formed recollection in response to at least one of the 24 cue words. This observation suggests that, despite extensive prompting and encouragement by the interviewers to produce a narrative, participants sometimes failed to do so rather than produce a fictitious story.

Autobiographical Memory Interview

Memory was assessed for autobiographical incidents and facts from childhood using the autobiographical memory interview (AMI). The patients performed similarly to the controls in all respects. For the patients, the

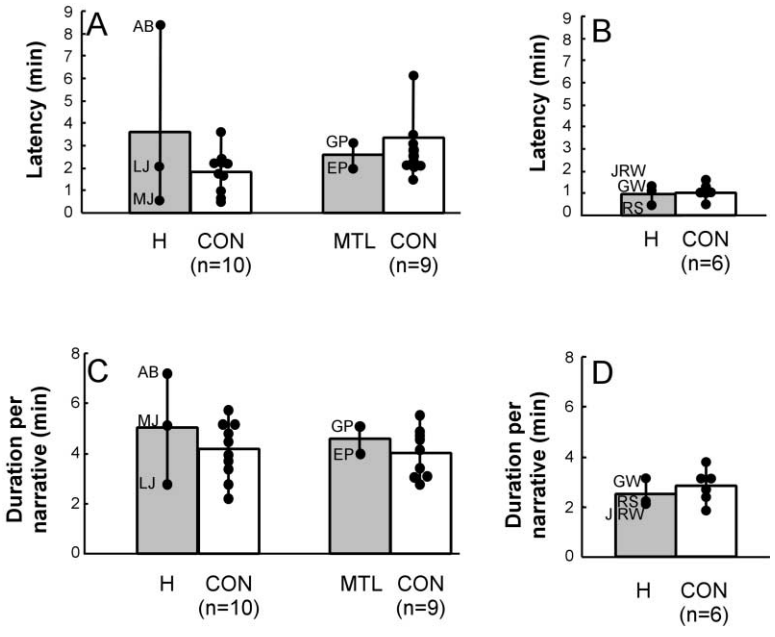

Figure 6. The Latency and Duration of the Remote Autobiographical Memories Given by Patients and Controls

Panels (A) (first study) and (B) (second study) show the time needed after the presentation of a cue word to begin a well-formed narrative. Panels (C) (first study) and (D) (second study) show the mean duration of the narratives. Abbreviations as in Figure 3.

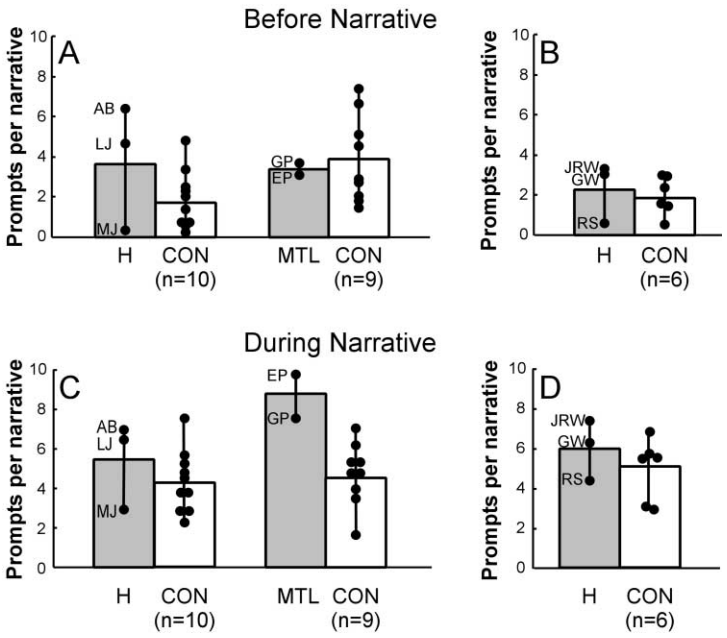

Figure 7. The Number of Prompts Given by the Interviewer to Patients and Controls before and during Recall of Remote Autobiographical Memories

Panels (A) (first study) and (B) (second study) show the mean number of prompts given before each narrative was begun. Panels (C) (first study) and (D) (second study) show the mean number of prompts given during the narratives themselves. Abbreviations as in Figure 3.

mean score for autobiographical incidents from childhood was 8.9, range = 8–9 (controls, 7.9, range = 5–9; maximum score = 9). For personal facts, the mean patient score was 18.9, range = 13.5–21 (controls, 17.8, range = 8–21; maximum score = 21).

Discussion

Six patients with damage limited primarily to the hippocampal region and two patients with more extensive damage to the medial temporal lobe were able to recollect detailed autobiographical memories from their early life. In comparison to 25 controls, the narratives of the patients contained a similar number of details about specific events (episodic details) and a similar number of background facts (semantic details) (Figure 4). Followup assessments suggested that the narratives were recollections from memory rather than fabrications.

The patients and controls also performed similarly in other respects. Thus, once the cue word was presented, the patients and controls required a similar amount of time to search for and begin the telling of a suitable recollection (2.4 min versus 2.2 min; Figures 6A and 6B); and once a recollection was begun, the patients and controls took a similar amount of time to report it (4.0 min versus 3.8 min; Figures 6C and 6D). Further, the patients and controls received a similar number of prompts before beginning their recollections (Figures 7A and 7B). Finally, the patients and controls also performed equivalently on the childhood portion of the AMI.

Sem **Sem** **Sem**
Dad had 3 ½ acres of property/ in Castro Valley/ and the back property would just grow/

Sem **Epi** **Epi**
and would be dry /and for some reason, I didn't do it, but somehow or other,/ the next thing we

Epi **Epi**
knew is that it was starting to burn. /I told dad/ and he called the Castro Valley fire department./

Epi **Epi** **Epi** **Rep**
They came up/ and they got it out real quick./ However it started I don't know./ He had 3 ½ acres

Rep **Sem** **Rep**
of property /and he just let it grow./ It would be grass or whatever./ Who knows how it started,

Rep **Rep** **Rep** **Epi**
/but it started to burn./ Dad called the Castro Valley fire department /and they came up /and all

Epi **Epi**
the volunteers came in/ and they got it out in a matter of 10-15 minutes./ They stamped it out./

Rep **Epi** **Rep**
They don't know how it started./ I was 16-17, in that bracket./ Dad had 3 ½ acres of property./ It

Epi **Epi**
was summer time,/ 1938/ Those sort of things I think you remember.

Figure 8. An Example of the Scoring Technique

The text printed here represents the response to the cue word "fire" by patient E.P. (Epi, episodic detail; Sem, semantic detail; Rep, repetition). For this narrative, no prompts were needed before the recollection was begun, and five prompts were given during the recollection.

Although this test is less sensitive than the other measures of autobiographical memory reported here, it is standardized and permits direct comparisons with patients tested in other settings.

The only differences that emerged between the patients and the controls were that the patients received more prompts than the controls during the reporting of their autobiographical recollections (Figures 7C and 7D) and also repeated details within a narrative more often than the controls (Figure 5). These differences were due to the performance of E.P. and G.P. (the two patients with the most extensive medial temporal lobe damage) and were not apparent in comparisons between the other six patients and their controls.

These findings for autobiographical memory are consistent with the results of earlier studies of patients R.B., L.M., and W.H., where damage to the hippocampal formation was documented by neurohistological analysis (Zola-Morgan et al., 1986; MacKinnon and Squire, 1989; Rempel-Clower et al., 1996). Patient H.M., who has large medial temporal lobe lesions (Corkin et al., 1997), has also been described as being able to recall personal episodes, which were restricted to the period when he was younger than 17 (Sagar et al., 1985), though uncertainty remains about whether he can perform normally in this regard (Corkin, 2002). More recent studies have also reported good remote memory for autobiographical episodes in patients with hippocampal damage (Reed and Squire, 1998; Kapur and Brooks, 1999; for an additional possible single case, see Fujii et al., 1999). However, all these studies characterized remote memory only qualitatively or assessed recollections by scoring them on a 0 to 3 scale. The present study documents intact remote memory in patients with medial temporal lobe damage using detailed quantitative analysis of narrative content and other measures of narrative performance.

In striking contrast to the results described here, a few patients have been reported to have difficulty recalling autobiographical episodes, even from their early life (five patients; Moscovitch et al., 2000; patient V.C.; Cipolotti et al., 2001; patient Y.K.; Hirano and Noguchi, 1998). One study (Moscovitch et al., 2000) included the extensively studied patient K.C., whose memory impairment was caused by a head injury that damaged the frontal, parietal, and occipital cortices in addition to the medial temporal lobe (Tulving et al., 1991). For the four other patients tested with K.C., little anatomical information is available (two had lesions outside the medial temporal lobe, one had early Alzheimer's disease, and one had amnesia following encephalitis). The relevance of these patients to the function of the hippocampus and related medial temporal lobe structures is therefore difficult to determine (for additional discussion of K.C., see Bayley and Squire, 2002).

Two other patients were also reported to be impaired at recalling autobiographical episodes. Patient Y.K. (Hirano and Noguchi, 1998) failed to produce a single autobiographical episode in response to 12 cue words of the kind used in the present study, and he also performed poorly (4 points out of 9) on the childhood portion of the AMI. A magnetic resonance imaging (MRI) scan was interpreted as showing restricted bilateral hippocampal damage, but in view of the etiology (thought to be encephalitis), quantitative analysis of regional brain volumes would be useful to assess the possibility that additional damage has occurred.

Patient V.C. (Cipolotti et al., 2001) developed memory impairment following episodes of cerebral ischemia accompanied by seizures. He was severely impaired in the AMI, obtaining only 1 out of 9 points on the childhood portion of the test. Quantitative analysis of MRI scans showed reduced volume in the hippocampus bilaterally (45%), the left entorhinal cortex (28%), and the left parahippocampal gyrus (31%). Temporal lobe volume was reported to be normal. Measurements were not reported for frontal, parietal and occipital lobes. In the present context, the striking finding in both single-case studies is that these two patients (Y.K. and V.C.), whose medial temporal lobe damage is less extensive than the damage in E.P. and G.P., nevertheless performed much more poorly on the autobiographical memory interview than did E.P., G.P., or any of the other six patients who participated in the present study. Accordingly, it is unlikely that the poor autobiographical memory ability of Y.K. and V.C. can be attributed to damage in the hippocampus itself, and it is doubtful as well that damage within the medial temporal lobe is solely responsible for their impairment. We suggest that patients who have difficulty recollecting well-formed episodic memories from early life will ultimately prove to have damage outside of the medial temporal lobe.

It should be noted that our results count against the recently proposed multiple-trace theory (MTT) of memory, which states that the hippocampus and related structures are always necessary for recalling the richness of detail that is characteristic of autobiographical episodic memory (Nadel and Moscovitch, 1997; Moscovitch et al., 2000). Our findings with patients E.P. and G.P. are especially relevant to this point, as these patients have large, nearly complete medial temporal lobe lesions which spared only the posterior aspect of the parahippocampal cortex. According to the MTT, these two patients would be expected to be particularly deficient at recalling richly detailed autobiographical memories. Yet, these two patients were able to produce well-formed autobiographical memories like the controls and like the other patients with more limited medial temporal lobe damage.

What brain regions beyond the medial temporal lobe might support the capacity for autobiographical remembering of remote episodes? One candidate is lateral temporal neocortex. Patient G.T. (not in the present study) developed profound amnesia following encephalitis, which damaged the medial temporal lobe bilaterally (Schmolck et al., 2002). Unlike patients E.P. and G.P., G.T. was markedly deficient at reporting well-formed autobiographical memories from any part of his past life, and he scored 0 out of 9 points on the childhood portion of the AMI (Reed and Squire, 1998). The most striking difference among these patients, with respect to neuropathology, is that G.T.'s damage (but not E.P.'s or G.P.'s) extended laterally to involve the anterior 6 cm of the entire temporal lobe. Damage to lateral temporal cortex is known to degrade remote episodic memory and to severely impair scores on the childhood portion of the AMI (Graham and Hodges, 1997).

Another important region is frontal cortex, which supports the strategic aspects of recall as well as active or

Table 1. Characteristics of Amnesic Patients

Patient	Age (Years)	Education (Years)	WAIS-III IQ	WMS-R Attention	Verbal	Visual	General	Delay
A.B.	60	20	107	87	62	72	54	<50
L.J.	60	12	101	105	83	60	69	<50
M.J.	61	16	139	125	62	93	62	<50
E.P.	76	12	98	94	57	82	61	56
G.P.	55	16	98	102	79	62	66	<50
R.S.	45	12	99	99	85	81	82	<50
G.W.	43	12	108	105	67	86	70	<50
J.R.W.	39	12	90	87	65	95	70	<50

Note. The Wechsler Adult Intelligence Scale-III (WAIS-III) and the Wechsler Memory Scale-Revised (WMS-R) (Wechsler, 1987) yield mean scores of 100 in the normal population with a standard deviation of 15. The WMS-R does not provide numerical scores for individuals who score below 50. IQ scores for R.S. and J.R.W. are from the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981).

effortful reconstructive processes (Kopelman, 2002). In one study, 15 patients with pathology thought to be limited to the frontal lobes exhibited a marked impairment in recalling autobiographical memories (Kopelman et al., 1999). Finally, the occipital lobes can be important in autobiographical recollection. Eleven patients with occipital lesions who were impaired at forming visual images were also impaired at constructing well-formed autobiographical memories from their past, presumably because the experience of recollecting an event depends importantly on the successful retrieval of visual images (Rubin and Greenberg, 1998).

These considerations, together with the present findings, lead to the conclusion that damage to neocortex and not the medial temporal lobe is responsible for impaired autobiographical memory of remote events. However, it is important to qualify this conclusion in two ways. First, it is not possible to conclude that remote autobiographical memory is entirely intact in the patients with medial temporal lobe damage studied here. Although we were unable to distinguish qualitatively or quantitatively the recollections of patients from those of controls, it is possible that the patients were deficient in some way that escaped our analysis. At the same time, the present results clearly rule out the notion that patients with medial temporal lobe lesions are grossly deficient at autobiographical remembering. Indeed, test procedures less sensitive than those used here have readily detected impairment in the ability to recollect recently formed autobiographical memories (Beatty et al., 1987; Schnider et al., 1995; Mayes et al., 1997, Reed and Squire, 1998; Henke et al., 1999; Kapur and Brooks, 1999). Further, our procedures readily detected impairment in patient G.T., whose damage includes lateral temporal cortex.

Second, it is difficult to determine to what extent the narrative recollections reported by the patients can be termed episodic memories in the same sense as the rich and unique recollections that healthy individuals can readily recall from their very recent past. Yet, it is also true that it is difficult to make this determination in the case of the remote recollections reported by the controls. We can conclude only that the qualities that one finds in the remote recollections of healthy individuals are also found in the recollections of memory-impaired patients. One interesting possibility is that memories take on different characteristics as they become more remote; for example, memories may become more semantic, more fact-like, and less episodic. On the basis of studies of the severely amnesic patient S.S. (S.S. has extensive medial temporal lobe damage and some lateral temporal damage as well; Verfaellie et al., 2000), Cermak (1984) proposed that remote memory in amnesia consists nearly entirely of often-told stories that have become disconnected from their original temporal context and are now part of a personal base of semantic knowledge. If this proposal has application to patients with restricted medial temporal lobe damage, we would extend it by suggesting that the idea applies similarly to the remote memory of healthy individuals.

These considerations about the nature of remote memory notwithstanding, the empirical question at issue in the present study is whether remote autobiographical memory in patients with medial temporal lobe lesions is or is not deficient in comparison to the remote autobiographical memory of intact individuals. The present results indicate that memory-impaired patients with medial temporal lobe lesions can recollect detailed autobiographical memories from their remote past just as intact individuals can. Given the extensive evidence that autobiographical memories formed shortly before the onset of amnesia are impaired (Beatty et al., 1987; Schnider et al., 1995; Mayes et al., 1997, Reed and Squire, 1998; Henke et al., 1999; Kapur and Brooks, 1999), the results are consistent with the idea that the capacity for autobiographical recollection becomes independent of medial temporal lobe structures with the passage of time after learning.

Experimental Procedures

Participants

Study 1

Three amnesic patients (A.B., M.J, and L.J., two male) with damage limited primarily to the hippocampal region and two patients (E.P. and G.P., both male) with more extensive damage to the medial temporal lobe participated in the study (Table 1). Their anterograde amnesia was documented by their impaired delay recall performance and by poor paired-associate learning. They obtained scores of 27.8 and 3.2 for the copy and delayed (12 min) reproduction of the Rey-Osterrieth Complex Figure (controls = 30.3 and 20.6; Squire et al., 1989). Paired-associate learning (ten word pairs per trial for three trials) averaged 0.8, 1.2, 1.6 (controls = 6.0, 7.6, 8.9; Squire and Shimamura, 1986). Nineteen employees or volunteers (15 male) at the San Diego Veterans Affairs Healthcare System served as controls (CON) in this study. Three to six controls were matched to

each patient with respect to gender, age (CON = 65.9 years, range = 55–80 years), and education (CON = 14.4 years, range = 12–20 years).

Study 2

Three male amnesic patients (J.R.W., G.W., and R.S.) with damage limited primarily to the hippocampal region and six male controls participated in the second study (Table 1). The first and second study were identical except that different interviewers were used. In addition, the participants in the second study averaged 22.8 years younger than the participants in the first study.

The three patients in study 2 obtained scores of 29.3 and 1.7 for the copy and delayed (12 min) reproduction of the Rey-Osterrieth figure. Paired-associate learning (ten word pairs per trial for three trials) averaged 0, 0.7, 1.3. Two controls were matched to each patient with respect to gender, age (CON = 42.3 years, range = 38–49 years), and education (CON = 12.3 years, range = 12–14 years).

The ages at which the eight patients in the two studies became amnesic are shown in Figure 1. Patients A.B. and J.R.W. became amnesic in 1976 and 1990, respectively, following an anoxic episode associated with cardiac arrest. R.S. and G.W became amnesic in 1998 and 2001, respectively, following a drug overdose and respiratory failure. L.J. became amnesic in 1988 during a 6 month period with no known etiology. Her memory impairment has been stable since that time. M.J. had a 10 year history of cardiovascular disease. Subsequently, in 1996, he awoke from a night's sleep complaining of memory difficulties. His memory impairment has remained stable since that time. Two of the patients (E.P. and G.P.) became amnesic in 1992 and 1987, respectively, after contracting viral encephalitis (Stefanacci et al., 2000; Schmolck et al., 2002).

For seven of the eight amnesic patients in the two studies, damage to the medial temporal lobe was quantified by structural magnetic resonance imaging (MRI) in a 1.5T clinical scanner (Figure 2). For the five patients in the two studies with damage restricted primarily to the hippocampal region, the volumes of the full anterior-posterior length of the hippocampus and the parahippocampal gyrus were measured using criteria based on histological analysis of healthy brains (Amaral and Insausti, 1990; Insausti et al., 1998). For each patient, the hippocampal and parahippocampal gyrus volumes were divided by the intracranial volume to correct for brain size (for L.J., only areal measurements based on coronal sections were available). Using this method, L.J., M.J., J.R.W., G.W., and R.S. had an average bilateral reduction in hippocampal volume of 28%, 10%, 29%, 45%, and 40%, respectively, relative to the volumes computed for age and gender-matched healthy controls (three to four new controls for each patient). The average bilateral reduction in the volume of the parahippocampal gyrus was 15%, 3%, 0%, 15%, and +3% (i.e., larger in the case of R.S.). Patient A.B. is unable to participate in MRI studies but is thought to have hippocampal atrophy on the basis of etiology and a neurological examination indicating well-circumscribed amnesia. In addition, high-resolution computed tomography (CT) images obtained in 2001 were consistent with damage restricted to the hippocampal region (Schmolck et al., 2002).

The two encephalitic patients (E.P. and G.P.) have more widespread damage to medial temporal lobe structures. E.P.'s hippocampal damage is virtually complete, and nothing remains of the hippocampus except a small tag of abnormally appearing vestigial tissue on each side approximating 10% of the hippocampal volume. The abnormal appearance of this tissue and the absence of entorhinal cortex (which originates the major cortical afferents to the hippocampus) make it unlikely that the remnant tissue is functional. His damage also extends caudally from the temporal pole to involve bilaterally all of the amygdaloid complex, all of the entorhinal and perirhinal cortices, and much of the parahippocampal cortex (20% on the left, and 60% on the right). At the level of the amygdala, the damage extends lateral to the parahippocampal gyrus to include the anterior fusiform gyrus (40% on the left, 53% on the right). Finally, the lateral temporal cortex and the insula are somewhat reduced in volume bilaterally (19% and 13% reductions, respectively).

G.P.'s damage is primarily in the medial temporal lobe, but his lesion extends further laterally than E.P's. The damage extends medially through the anterior 7 cm of the left temporal lobe and the anterior 6 cm of the right temporal lobe, including bilaterally all of the amygdala, all of the hippocampal region, all of the entorhinal and perirhinal cortices, and much of the parahippocampal cortex (77% on the left, 17% on the right). Lateral damage is most severe in the anterior 1 cm of the temporal lobe, where it includes the fusiform gyrus and the inferior, middle, and superior temporal gyri. The damage to the fusiform gyrus and the inferior temporal gyrus continues caudally 1 cm to 4.5 cm. There is also bilateral damage to the insular cortex, with the lesion extending caudally on the left side (3 cm) more than on the right side (2.5 cm) (Schmolck et al., 2002).

Procedure

Autobiographical memories were elicited using a modified version of the Crovitz test of autobiographical memory (Crovitz and Schiffman, 1974). Figure 1 illustrates the age of each patient at the time of testing and the portion of life from which memories were drawn. Patients were asked to recall events from the first third of their lives before the onset of amnesia, and the controls matched to each patient were queried from an equivalent portion of their lives. A list of 24 high-frequency nouns (e.g., river, bird, nail) was presented (one word at a time) with the instruction to recollect a unique event from the past that involved the stimulus word. Thus, participants produced a maximum of 24 narratives during their test sessions (mean = 2.4 test sessions, range = 1–7). All the test sessions were tape recorded for later scoring.

Specific instructions were as follows: "I am going to give you a word, and I would like you to tell me something that is connected with that word which happened to you one time during the time period zero to __ years old [each participant was assigned an age as illustrated in Figure 1]. The memory can be anything, as long as it happened to you, not something that you heard about from someone else." If the participant was unable to provide a memory that was specific in time and place, then prompts were given as follows.

Prompts (Before the Narrative Recollection Was Begun)

Prompts were given as needed before the participant began to describe a specific event. For example, to help the participant remember an event involving the cue word "lake," the interviewer might ask "Perhaps you remember one day when you went swimming in a lake?"

Prompts (During the Narrative Recollection)

Once the participant began to describe an event, prompts were given as needed in order to elicit more details. For example, the interviewer might ask "You said that you graduated from high school. Can you tell me more about the day you graduated?" or "What did you do after the graduation ceremony?"

More specific prompts were also given to try to elicit as much detail as possible (e.g., "What was the name of the racehorse who won the race you were watching?"). Prompts continued until the interviewer judged that the participant had recalled as many details as possible. Similar methods for eliciting autobiographical memories have been described in other studies (Moscovitch et al., 2000; Levine et al., 2002).

Autobiographical Memory Interview

In order to permit some comparison between our patients and patients tested in other settings, the eight amnesic patients and 13 new controls (nine male; age = 65.6 years; education = 14.6 years) were also assessed with the autobiographical memory interview (Kopelman et al., 1989). This standardized test quantifies the recall of autobiographical incidents and personal facts from childhood (until age 18) and two later time periods. Following published procedures, participants were asked to recall three unique events from childhood (autobiographical incidents) and 12 facts about childhood (personal facts).

Scoring

Scoring of the tape-recorded narratives was accomplished in two stages. First, all narratives were scored on a 0 to 3 scale. This scale was used to permit comparison with previous studies that used this test (Zola-Morgan et al., 1983; MacKinnon and Squire, 1989; Reed and Squire, 1998) and also to identify well-formed narratives that were unique for time and place. Second, the well-formed narratives (i.e., ones given a 3 point score) were analyzed further to determine the total number of details they contained and to characterize them in other ways as well (latency, duration, number of prompts given, and repetitions; see below).

0 to 3 Scale

All narratives were first scored on a 0 to 3 scale (Zola-Morgan et al., 1983). Three points were awarded for an episodic memory that was specific to time and place (e.g., a description of the events on the day the participant passed the driving test). Two points were awarded for a memory that had some specificity but was not specific to one time and place and was therefore not recalled as a unique event (e.g., "I used to stay at my grandma's house on weekends."). One point was awarded for a vague reference to a memory but without any time or place reference (e.g., "I read a lot of books."). Zero points were given for no response or for a generic response (e.g., "You can open and close a door.").

Scoring for Detail

Narratives that received the maximum score of 3 points were further scored for the number of details that they contained. A detail was defined as a single unit of information such as an observation, thought, or event. As a result, a detail was usually several words in length but less than a sentence. Similar techniques have been used to segment prose for quantitative analysis (e.g., Johnson, 1970; Logical Memory subtest of the Wechsler Memory Scale-Revised [WMS-R]; Wechsler, 1987; Moscovitch et al., 2000; Levine et al., 2002).

Two categories of detail were defined: episodic detail and semantic detail. An episodic detail was a bit of information unique to an event and restricted to a specific time and place (e.g., the outcome of a particular sporting event played at school one day). In contrast, a semantic detail was information that was not unique to the event but that was nevertheless relevant to the narrative (e.g., the name of the school). The score for each participant was the number of episodic and semantic details reported in each narrative. Repetitions of the same details within a narrative were also counted (and not credited toward the participant's score for narrative content). An example of the scoring technique is shown in Figure 8.

Reliability of Scoring

The narratives from all 33 participants were scored for detail from the tape-recorded sessions by one rater. To determine the reliability of the scoring method, narratives from ten participants (four amnesic patients and six controls) were also scored by a second, independent rater. For both patients and controls, the second rater counted more details in the narratives than did the first rater (mean difference $= 5.5 \pm 1.1$ details per narrative). Nevertheless, the important observation was that both raters scored the patients and the controls similarly. The difference between the mean number of details per narrative recorded for the patients and the mean number of details per narrative recorded for the controls was 2.5% for the first rater and 3.0% for the second rater.

Latency to Begin a Narrative

The time between the presentation of a cue word and the beginning of each autobiographical memory was measured. During this period, the participant searched for an appropriate recollection, receiving prompts as needed. Thus, the latency measure covered the time period up until the participant began to report a well-formed 3 point narrative that contained episodic time-and-place information.

Duration of Narrative

The duration of the narrative was the time taken by the participant to report the narrative recollection. The time during which participants received instructions and the time taken by the participant for conversation not relevant to the narrative were excluded.

Prompts per Narrative

The number of prompts given by the interviewer was also recorded. Prompts given before the narrative recollection was begun were scored separately from prompts given during the narrative recollection.

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